perinatal cerebral infarction, unexpected premature delivery or an unexplained accident of pregnancy such as an abruption, maternal substance abuse must be placed in the differential diagnosis. An irritable newborn or one with unusual complications should be assessed with a full historical evaluation for substance exposure and, when indicated, a full toxicologic urine screen. Pediatricians have come to realize that intrauterine drug exposure has become a major cause of perinatal morbidity and mortality and an area that can no longer be overlooked.[6]

The developmental risks imposed by the maternal use of substances of abuse are, perhaps more than many other risk factors, preventable. The first step in prevention and intervention, however, relies on the establishment in the medical and public sectors of a perception of risk. This perception should be based on education of the public as to the clear effects maternal substance abuse has on pregnancy and neonatal outcome. Second, the medical and psychological communities must begin to better understand risk-taking behavior and the personality and motivational factors that engender and enhance this behavior. We must delineate the measurable outcomes that best express the damage of maternal substance abuse to the child, then use the most effective means of increasing the public's recognition of this risk and influencing the individual's will to act to reduce relevant risk-taking behavior.

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Myocarditis and Dilated Cardiomyopathy

ACUTE MYOCARDITIS is a clinical diagnosis that can be made with confidence when a previously healthy child or young adult has a new onset of abnormal cardiac function—as reflected in left or right (or both) ventricular failure, serious ventricular arrhythmia, or conduction disturbance—in the setting of an acute febrile illness specifically associated with a known microorganism such as measles, infectious mononucleosis, mycoplasma infection, trypanosomiasis[1] and in the absence of cardiodepressant drugs, toxins, or other systemic disease. As a rule, because of the generally benign course—often even subclinical—such cases rarely come to the attention of an internist or cardiologist. The diagnosis of myocarditis is facilitated by the presence of tachycardia out of proportion to fever and systemic illness, by evidence of pericarditis, by myositis, and by epidemiologic evidence of exposure to cardiotropic microorganisms. Notwithstanding the availability of rather safe methods of obtaining myocardial tissue for histopathologic study, relatively few patients have undergone myocardial biopsy in this acute setting. In young age groups, the exclusion of other forms of heart disease by other than general clinical means is hardly necessary, whereas in older persons the possibility of silent coronary artery disease or preexistent chronic subclinical cardiomyopathy must always be considered.

While the majority of such patients survive and go on to full clinical recovery, a significant number of patients observed carefully have shown clinical evidence of a chronic cardiomyopathy.[2,3] In one subset, ongoing myocardial inflammatory lesions found by myocardial biopsy on autopsy justify the diagnosis of subacute or chronic myocarditis,[4] whereas another subset of patients manifests dilated cardiomyopathy without histologic evidence of active myocarditis.[5]

This wide spectrum of the natural course of acute infection involving the myocardium mandates close follow-up of all patients with acute myocarditis for late stable or progressive myocardial dysfunction, which may for a long time remain subclinical. When present, however, this disorder should dictate appropriate therapy and especially secondary prevention by control of preload and afterload—including restriction of activity in some cases—and by protection of the person from cardiotoxins such as ethanol.

It is, however, another group of patients who come to the attention of internists and cardiologists with considerably greater frequency, namely, patients who have experienced a relatively recent onset of congestive heart failure without a history of acute myocarditis and who, in the absence of evidence of congenital, valvular, coronary artery, or specific heart muscle disease, are diagnosed as having dilated cardiomyopathy. An endomyocardial biopsy is frequently carried out in this patient group and, depending on the population sampled, the number of specimens taken, and the pathologic criteria used, a significant percentage are diagnosed as having active myocarditis. It is this type of patient that is discussed elsewhere in this issue. O'Connell and Mason present a comprehensive review of both clinical and experimental evidence for the infectious-immune cause of chronic, dilated cardiomyopathy. According to this concept, whereas the initial myocardial disease is directly related to the infectious agent, usually a virus, the ensuing progressive myocardial damage and fibrosis, with or without persistent inflammation, is attributable to immune or autoimmune processes. One may wonder why, in view of the multifaceted evidence presented, the infectious-immune cause of some cases of dilated cardiomyopathy continues to be labeled as a hypothesis for which evidence remains circumstantial.

In individual inbred strains of mice, the myocardial response to acute experimental infection with a specific strain of a specific virus tends to be remarkably uniform, but there is a wide variation of expression of the response in different strains.[6,7] Thus, it is entirely unreasonable to expect a uniform response to acute viral infections in humans, an outbred species, exposed to many different viruses and even strains of viruses. We are not surprised, then, at the wide spectrum of clinical expression seen in acute outbreaks of viral disease. A similar wide spectrum of myocardial involvement has recently been observed in an outbred animal—the pig—exposed to a myotropic strain of encephalomyocarditis virus.[8] In this connection, the reports of familial myocarditis quoted by O'Connell and Mason are also relevant.

With regard to the diagnosis of myocarditis, we may be disadvantaged by the definition of myocarditis as an inflam-

matory reaction of the myocardium, a definition reemphasized by the criteria developed by Aretz and colleagues, which base the diagnosis on the histopathologic demonstration of coexisting myocyte necrosis and cellular infiltration.[9] Without denying the clinical value if not necessity of diagnostic standards such as the Dallas criteria, we wonder if our understanding of the biology of the cardiac effects of viral infections and associated immune or autoimmune reactions may not be better served by keeping an open mind with regard to the morphologic and functional expressions of viral and immunologic effects on the heart. Viruses may also invade interstitial cells such as fibroblasts, as well as vascular smooth muscle cells. The effects of such involvement on cardiac function have hardly been explored, although recently the cytoskeleton has been given some attention in the pathogenesis of dilated cardiomyopathy.[10]

Such concepts might lead to surveys of patients with acute viral disease by means of radionuclide studies such as antimyosin scans,[11] along with noninvasive assessments of cardiac function such as echocardiograms and radioventriculograms, and with endomyocardial biopsies, with follow-up to determine the incidence of later evidence for dilated cardiomyopathy.

As a logical result of the increasing evidence for a role of the immune system in ongoing subacute and chronic myocardial inflammatory processes, immunosuppressive therapy has come into increasing clinical use, not only in patients with biopsy results positive for active myocarditis, but also in patients with dilated cardiomyopathy of recent onset. In view of the absence of proof of the effectiveness and the significant side effects of immunosuppressive agents, the controlled randomized trial described by O'Connell and Mason is of the utmost importance. The considerable differences in immunologic processes found in different strains of inbred mice,[6,7] however, suggest that immunosuppressive therapy with one agent may not be uniformly effective. It is hoped that the simultaneous study of indices of humoral and cellular immunopathogenetic factors will permit an analysis of the effect of immunosuppressive therapy in relation to subgroups of patients. It would be erroneous, however, to conclude that the immune system has only a deleterious effect on the myocardium in this disease. Studies of experimental viral infection in mice have shown that suppression of the immune system during the viremic phase of the infection may enhance myocardial replication of virus and myocardial damage.[12,13] Thus, immunosuppressive therapy should not be considered during the acute viremic phase of a viral myocarditis.

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The Fetus as Patient

A GENERATION AGO the human fetus seemed a mystery, hidden within the walls of the uterus and far removed from the efforts of diagnostic and therapeutic medicine. This began to change in a significant way with the advent of amniocentesis in cases of Rh isoimmunization in the 1950s, followed by genetic amniocentesis in the 1960s to determine the fetal chromosomal status. By the 1970s, sonographic imaging of the fetus had matured to the point of providing detailed and clinically useful anatomic information within the womb. It could truly be said that the walls separating the physician from the fetus had crumbled and that during pregnancy there now were two patients calling on the skill and technology of modern medicine, the mother and her unborn baby.

The rapid progress in fetal medicine has been exciting to its practitioners and to most families who seek medical information about their unborn babies. As of the present, diagnostic efforts have greatly outstripped therapeutic ones on behalf of the fetus, however. This situation is not unexpected and parallels most other new areas in medicine. A future era of expanded fetal therapeutic options will stand rightfully on an established understanding of normal fetal development and physiology and the refined ability to make correct diagnoses.

A concomitant of rapid progress is a certain level of confusion in other areas of society, including the law, as to the meaning and implications of fetal medicine. Debates have sprung up about the existence and extent of a fetal right to medical intervention, about possible expected behaviors of a mother vis-à-vis her fetus, and about the means of resolution or adjudication if there seems to be a conflict between maternal (or paternal) and fetal interests. Controversy about elective abortion greatly complicates these questions. It is likely that we will have continued unrest surrounding these issues for quite some time.

The success of prenatal diagnosis has coincided with the willingness to go to the fetus—that is, to enter the womb for diagnostic testing. From the point of view of risks and complications to the fetus and pregnancy, it would be preferable to stay outside of the womb and make do with maternal blood and urine specimens, abdominal palpation and auscultation, or other innocuous examinations. With the exception of measurements of maternal serum α-fetoprotein concentrations, this safest approach has not yet been fruitful for the diagnosis of fetal disease. Even so, it is axiomatic that the least invasive modality of fetal examination be chosen consistent with being able to accomplish a desired diagnosis.

One can draw obvious parallels in the diagnostic ap-